

IN THE CLAIMS:

Kindly amend the claims as follows:

- 1 1. (Previously Amended) A method of detecting a
2 malignant tumor in a human subject, comprising:
3 (a) collecting a sample of a bodily substance containing human
4 nucleic acid ~~or protein~~, said nucleic acid ~~or protein~~ having
5 originated from cells of the human subject;
6 (b) detecting quantitatively or semi-quantitatively in the sample
7 a level of expression for ~~laminin α 4 subunit protein or~~
8 laminin α 4-specific mRNA; and
9 (c) comparing the expression level in (b) to a level of
10 expression in a normal control, wherein overexpression of
11 ~~laminin α 4 subunit protein~~ or laminin α 4-specific mRNA,
12 with respect to the control, indicates the presence of a
13 malignant tumor in the human subject.

- 1 2. (Currently Amended) The method of Claim 1, wherein
2 the bodily substance is blood, urine, lymph, cerebro-spinal fluid, skin, stroma,
3 vascular epithelium, oral epithelium, vaginal epithelium, cervical epithelium,
4 uterine epithelium, intestinal epithelium, bronchial epithelium, esophageal
5 epithelium, or mesothelium.

- 1 3. (Currently Amended) The method of Claim 1, wherein
2 the bodily substance is a tissue sample.

1 4. (Original) The method of Claim 3, wherein the tissue
2 sample is collected from the brain of the subject.

1 5. (Original) The method of Claim 3, wherein the tissue
2 sample is a tumor tissue.

1 6. (Original) The method of Claim 1, wherein the bodily
2 substance is plasma.

1 7. (Original) The method of Claim 1, wherein the bodily
2 substance is a cellular material.

1 8. (Original) The method of Claim 7, wherein the cellular
2 material is derived from the human subject's brain kidney, bladder, ureter,
3 urethra, thyroid, parotid gland, submaxillary gland, sublingual gland, lymph
4 node, bone, cartilage, lung, mediastinum, breast, uterus, ovary, testis,
5 prostate, cervix uteri, endometrium, pancreas, liver, spleen, adrenal,
6 esophagus, stomach, or intestine.

1 9. (Currently Amended) The method of Claim 4 I,
2 wherein the ~~neoplastic growth~~ cellular material is a carcinoma, sarcoma,
3 lymphoma, mesothelioma, melanoma, glioma, neuroblastoma, glioblastoma,
4 oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal
5 tumor, atypical meningioma, malignant meningioma, or neuroblastoma.

1 10. (Currently Amended) The method of Claim 4 ~~8~~,
2 wherein the cellular material is a hyperplastic and/or cytologically dysplastic
3 cellular growth or proliferation that is benign prostatic hyperplasia/dysplasia or
4 cervical hyperplasia/dysplasia.

Claims 11 and 12 have been cancelled

1 13. (Previously Amended) The method of Claim ~~12~~ 2,
2 wherein the expression level of laminin α 4-specific mRNA is detected by
3 measuring RNA.

1 14. (Previously Amended) The method of Claim ~~12~~ 2,
2 wherein the expression level of laminin 4-specific mRNA is detected by
3 measuring cDNA.

1 15. (Previously Amended) The method of Claim ~~12~~ 2,
2 wherein a gene expression microarray is used to detect the level of expression
3 of laminin α 4-specific mRNA.

1 16. (Previously Amended) The method of Claim 1, further
2 comprising detecting the overexpression of ~~laminin β 1 subunit protein or~~
3 laminin β 1 subunit protein or *laminin β 1*-specific mRNA relative to the normal
4 control.

1 17. (Original Claim) The method of Claim 1, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal control, of a gene encoding a protein
4 selected from the group consisting of insulin-like growth factor binding protein
5 precursor 3, transforming growth factor- β -induced gene, vascular endothelial
6 growth factor, connective tissue growth factor, human insulin-like growth
7 factor binding protein precursor 5, placental growth factor, transcription factor
8 Ap-2, human insulin-like growth factor II, epidermal growth factor receptor,
9 matrix metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase
10 A2 receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV α 1
11 chain, or detecting a combination of expression levels for any of these.

1 18. (Previously Amended) A method of diagnosing the
2 presence of a glioma in a human subject, comprising:
3 (a) obtaining a sample from the brain of the human subject;
4 (b) detecting quantitatively or semi-quantitatively in the sample
5 a level of expression for ~~laminin α 4 subunit protein or~~
6 *laminin α 4-specific mRNA*; and
7 (c) comparing the expression level in (b) to a level of
8 expression in a normal control, wherein overexpression of
9 ~~laminin α 4 subunit protein or~~ *laminin α 4-specific mRNA*,
10 with respect to the control, indicates the presence of
11 glioma in the subject.

Claims 19 and 20 have been cancelled.

1 21. (Previously Amended) The method of Claim 18 ~~20~~,
2 wherein the expression level of *laminin* α 4-specific mRNA is detected by
3 measuring RNA.

1 22. (Previously Amended) The method of Claim 18 ~~20~~,
2 wherein the expression level of *laminin* α 4-specific mRNA is detected by
3 measuring cDNA.

1 23. (Previously Amended) The method of Claim 18 ~~20~~,
2 wherein a gene expression microarray is used to detect the level of expression
3 of *laminin* α 4-specific mRNA.

1 24. (Previously Amended) The method of Claim 18, further
2 comprising detecting the overexpression of ~~laminin β 1 subunit protein or~~
3 *laminin* β 1-specific mRNA relative to the normal control.

1 25. (Original Claim) The method of Claim 18, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal control, of a gene encoding a protein
4 selected from the group consisting of insulin-like growth factor binding protein
5 precursor 3, transforming growth factor- β -induced gene, vascular endothelial
6 growth factor, connective tissue growth factor, human insulin-like growth
7 factor binding protein precursor 5, placental growth factor, transcription factor
8 Ap-2, human insulin-like growth factor II, epidermal growth factor receptor,
9 matrix metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase
10 A2 receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV α 1
11 chain, or detecting a combination of expression levels for any of these.

1 26. (Original Claim) The method of Claim 18, wherein the
2 sample is a tumor tissue.

1 27. (Original Claim) The method of Claim 18, wherein the
2 sample comprises plasma.

1 28. (Previously Amended) A method of predicting the
2 recurrence of a malignant tumor in a human subject from whom a tumor has
3 been resected, comprising:

4 (a) obtaining a tissue sample from the human subject, said tissue
5 sample being from a region adjacent to the site of the
6 tumor;

7 (b) detecting quantitatively or semi-quantitatively a level of
8 expression for ~~laminin α 4 subunit protein or laminin α 4-~~
9 specific mRNA in the sample; and

10 (c) comparing the expression level in (b) to a level of expression
11 in a normal tissue control, wherein overexpression of
12 ~~laminin α 4 subunit protein or laminin α 4-specific~~ mRNA,
13 with respect to the control, is predictive of a recurrence of
14 a malignant tumor in the subject.

1 29. (Original Claim) The method of Claim 28, wherein the
2 tissue sample is histopathologically normal in appearance.

Claims 30 and 31 have been cancelled.

1 32. (Previously Amended) The method of Claim 28 ~~31~~,
2 wherein the expression level of laminin α 4-specific mRNA is detected by
3 measuring RNA.

1 33. (Previously Amended) The method of Claim 28 ~~31~~,
2 wherein the expression level of laminin α 4-specific mRNA is detected by
3 measuring cDNA.

1 34. (Previously Amended) The method of Claim 28 ~~31~~,
2 wherein a gene expression microarray is used to detect the level of expression
3 of *laminin α 4*-specific mRNA.

1 35. (Original Claim) The method of Claim 28, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal tissue control, of a gene encoding a
4 protein selected from the group consisting of insulin-like growth factor binding
5 protein precursor 3, transforming growth factor- β -induced gene, vascular
6 endothelial growth factor, connective tissue growth factor, human insulin-like
7 growth factor binding protein precursor 5, placental growth factor,
8 transcription factor Ap-2, human insulin-like growth factor II, epidermal growth
9 factor receptor, matrix metalloproteinase-2, keratin 18, vimentin, fibronectin
10 1, phospholipase A2 receptor, desmoplakin, tropomodulin, tenascin C, and
11 collagen type IV α 1 chain, or detecting a combination of expression levels for
12 any of these.

1 36. (Previously Amended) The method of Claim 28, further
2 comprising detecting the overexpression of ~~laminin β 1 subunit protein or~~
3 *laminin β 1-specific mRNA* ~~nucleic acid~~ relative to the normal tissue control.

Claims 37-43 are cancelled.

1 44. (Previously Amended) A method of predicting the
2 recurrence of a glioma in a human subject from whom a glioma has been
3 resected, comprising:
4 (a) obtaining a tissue sample from the brain of the human
5 subject, said tissue sample being from a region adjacent to
6 the site of the glioma;
7 (b) detecting quantitatively or semi-quantitatively a level of
8 expression for ~~laminin α 4 subunit protein or~~ *laminin α 4-*
9 specific mRNA in the sample; and
10 (c) comparing the expression level in (b) to a level of expression
11 in a normal tissue control, wherein overexpression of
12 ~~laminin α 4 subunit protein or~~ *laminin α 4-specific mRNA*,
13 with respect to the control, is predictive of a recurrence of
14 glioma in the subject.

1 45. (Original Claim) The method of Claim 44, wherein the
2 tissue sample is histopathologically normal in appearance.

Claims 46-47 are cancelled.

1 48. (Previously Amended) The method of Claim 44 ~~47~~,
2 wherein the expression level of *laminin* α 4-specific mRNA is detected by
3 measuring RNA.

1 49. (Previously Amended) The method of Claim 44 ~~47~~,
2 wherein the expression level of *laminin* α 4-specific mRNA is detected by
3 measuring cDNA.

1 50. (Previously Amended) The method of Claim 44 ~~47~~,
2 wherein a gene expression microarray is used to detect the level of expression
3 of *laminin* α 4-specific mRNA.

1 51. (Original Claim) The method of Claim 44, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal tissue control, of a gene encoding a
4 protein selected from the group consisting of insulin-like growth factor binding
5 protein precursor 3, transforming growth factor- β -induced gene, vascular
6 endothelial growth factor, connective tissue growth factor, human insulin-like
7 growth factor binding protein precursor 5, placental growth factor,
8 transcription factor Ap-2, human insulin-like growth factor II, epidermal growth
9 factor receptor, matrix metalloproteinase-2, keratin 18, vimentin, fibronectin
10 1, phospholipase A2 receptor, desmoplakin, tropomodulin, tenascin C, and
11 collagen type IV α 1 chain, or detecting a combination of expression levels for
12 any of these.

1 52. (Previously Amended) The method of Claim 44, further
2 comprising detecting the overexpression of ~~laminin β 1 subunit protein~~ or
3 *laminin β 1*-specific mRNA ~~nucleic acid~~ relative to the normal tissue control.

1 53. (Original Claim) A method of predicting recurrence of a
2 glioma in a human subject from whom a glioma has been resected,
3 comprising:
4 (a) obtaining a tissue sample from the brain of a human
5 subject, said tissue sample being from a region adjacent to
6 the site of the glioma, said sample comprising a cell
7 expressing a plurality of mRNA species that are detectably
8 distinct from one another;
9 (b) detecting quantitatively or semi-quantitatively an
10 expression level for *laminin α 4*-specific mRNA; and
11 (c) comparing the expression level in (b) to a level of expression
12 in a normal tissue control, wherein overexpression of
13 *laminin α 4*-specific mRNA, with respect to the control, is
14 predictive of a recurrence of glioma in the subject.

1 54. (Original Claim) The method of Claim 53, wherein a
2 gene expression microarray is used to detect the level of expression of *laminin*
3 *α 4*-specific mRNA.

1 55. (Original Claim) The method of Claim 54, wherein the
2 expression level of *laminin α 4*-specific mRNA is detected by measuring RNA.

1 56. (Original Claim) The method of Claim 54, wherein the
2 expression level of *laminin* $\alpha 4$ -specific mRNA is detected by measuring cDNA.

1 57. (Original Claim) The method of Claim 53, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal tissue control, of a growth factor-
4 related gene encoding a protein selected from the group consisting of insulin-
5 like growth factor binding protein precursor 3, transforming growth factor- β -
6 induced gene, vascular endothelial growth factor, connective tissue growth
7 factor, human insulin-like growth factor binding protein precursor 5, placental
8 growth factor, transcription factor Ap-2, human insulin-like growth factor II,
9 and epidermal growth factor receptor, whereby the relative aggressiveness of
10 the glioma is predicted.

1 58. (Original Claim) The method of Claim 53, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal tissue control, of a structural gene
4 encoding a protein selected from the group consisting of matrix
5 metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase A2
6 receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV $\alpha 1$
7 chain, whereby the relative invasiveness of the glioma is predicted.

1 59. (Original Claim) The method of Claim 53, further
2 comprising detecting the overexpression of *laminin* $\beta 1$ -specific mRNA relative
3 to the normal tissue control.

- 1 60. (Presently Amended) A method of ~~classifying~~
2 establishing a ~~the~~ grade of a malignant tumor in a human subject, wherein said
3 grade ranks tumors in terms of invasiveness and aggressiveness, comprising:
4 (a) obtaining a tissue sample from the human subject, said
5 sample comprising a cell expressing a plurality of mRNA
6 species that are detectably distinct from one another;
7 (b) detecting quantitatively or semi-quantitatively an
8 expression level for at least two of the plurality of mRNA
9 species, wherein at least one of the detected mRNA
10 species is a *laminin* α 4-specific mRNA and at least one is
11 specific to a growth factor-related gene or to a structural
12 gene other than a laminin gene;
13 (c) constructing an expression profile of the sample comprising
14 a combination of the detected expression levels of *laminin*
15 α 4-specific mRNA and the at least one other mRNA species
16 specific to the growth factor-related gene or to the
17 structural gene other than a laminin gene; and
18 (d) comparing the expression profile in (c) to an expression
19 profile for a normal tissue control, wherein a level of
20 overexpression of *laminin* α 4-specific mRNA, with respect
21 to the control, is indicative of the presence of and ~~relatively~~
22 ~~high degree of~~ invasiveness of the tumor in the subject,
23 wherein a level of overexpression of the structural gene
24 other than a laminin gene, with respect to the control, is
25 indicative of ~~relatively high degree of~~ tumor invasiveness,
26 and wherein a level of overexpression of the growth factor-
27 related gene, with respect to the control, is indicative of

28 ~~relatively high~~ degree of tumor aggressiveness.
29

1 61. (Original Claim) The method of Claim 60, wherein the
2 growth factor-related gene encodes a protein selected from the group
3 consisting of insulin-like growth factor binding protein precursor 3,
4 transforming growth factor- β -induced gene, vascular endothelial growth factor,
5 connective tissue growth factor, human insulin-like growth factor binding
6 protein precursor 5, placental growth factor, transcription factor Ap-2, human
7 insulin-like growth factor II, and epidermal growth factor receptor.

1 62. (Original Claim) The method of Claim 60, wherein the
2 structural gene encodes a protein selected from the group consisting of matrix
3 metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase A2
4 receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV α 1
5 chain.

1 63. (Original Claim) The method of Claim 60, wherein the
2 expression level of *laminin* α 4-specific mRNA is detected by measuring RNA.

1 64. (Original Claim) The method of Claim 60, wherein the
2 expression level of *laminin* α 4-specific mRNA is detected by measuring cDNA.

1 65. (Original Claim) The method of Claim 60, wherein a
2 gene expression microarray is used to detect the level of expression of *laminin*
3 α 4-specific mRNA.

1 66. (Original Claim) The method of Claim 60, further
2 comprising detecting the overexpression of *laminin* $\beta 1$ -specific mRNA relative
3 to the normal tissue control.

1 67. (Original Claim) The method of Claim 60, wherein the
2 tissue sample is brain tissue.

1 68. (Original Claim) The method of Claim 60, wherein the
2 tumor is a glial tumor.

Claims 69-74 have been cancelled.

1 75. (Previously Added) The new method of Claim 1, further
2 comprising detecting the overexpression of a gene encoding laminin $\beta 1$ subunit
3 relative to the normal control.

1 76. (Previously Added) The method of Claim 18, further
2 comprising detecting the overexpression of a gene encoding laminin $\beta 1$ subunit
3 relative to the normal control.

1 77. (Previously Added) The method of Claim 28, further
2 comprising detecting the overexpression of a gene encoding laminin $\beta 1$ subunit
3 relative to the normal control.

1 78. (Previously Added) The method of Claim 44, further
2 comprising detecting the overexpression of a gene encoding laminin β 1 subunit
3 relative to the normal control.